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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,497	02/17/2000	DAVID J. FITZGERALD	015280-317100US	4036

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/381,497	Applicant(s) FITZGERALD	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-14,16,17,22-27 and 29-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-14,16,17,22-27 and 29-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 5, 11, and 12 have been amended.

Claims 1-5, 7-14, 16-17, 22-27, 29-32 are under examination.

2. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

3. The following Office Action contains some NEW GROUNDS of rejection.

Rejections Withdrawn

4. The rejection of claims 1-4, 7, 11, 22-26, 29-32 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendments to the claims.

Response to Arguments

5. the rejection of claims 1-5, 7-14, 16-17, 22-27, 29-32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

Claims 1 and 11 have been amended to recite the limitation a recombinant immunoconjugate... and has 90% or greater of the binding affinity of the prototype RFB4 dsFv". The response filed 11/8/02 has been carefully considured but is deemed not to

be persuasive. The response states that claims 1 and 11 are drawn to immunoconjugates comprising an RFB4 dsFv with the claimed specificity. This is supported in the indicated passage (page 15, lines 10-14) (see page 4-5 of response). In response to this argument, again at the cited page the specification is referring to a "RFB4 binding fragment" and no mention of an immunoconjugate is seen. There is no mention of an immunoconjugate with 95% sequence identity to SEQ ID NO:2 or 4 or the sequence in RFB4 dsFv. The claims encompass an immunoconjugate with the recited % affinity and this limitation is not seen at the cited page in the specification. Applicant is required to provide specific support for the limitation in the specification as originally filed or remove the limitation from the claims.

6. The rejection of claims 1-5, 7-14, 16-17, 22-27, 29-32 under 35 U.S.C. 103(a) as being unpatentable over Ghetie et al (Cancer Res. 51:5876-5880, 1991) and further in view of Shen et al (Int. J. Cancer 42:792-797, 1988) and Reiter et al (Biochemistry 33:5451-5459, 1994) and Kuan et al (Biochemistry 35:2872-2877, 1996, Abstract published 2/1/96) and Orlandi et al (Proc. Natl. Acad. Sci. USA, 86:3833-3837, 1989) is maintained.

The response filed 11/8/02 has been carefully considered but is deemed not to be persuasive. The response states "the Federal circuit has held that a nucleic acid sequence is not obvious over general methods of isolated cDNA or DNA molecules" (see page 6 of response). In response to this argument, while the statement may be true for a general nucleic acid sequence, as cited in Orlandi et al the homology in the

VH and VL genes primers can be made and were made to PCR out the VH and VL genes from five mouse hybridoma cells. Thus, while cloning of a general gene may not be obvious, cloning of antibody VH and VL genes from hybridoma cells were routine at the time of applicants claimed invention. This proposition that the references failed to teach the structure of the claimed antibody precludes the teachings thereof from serving as evidence to establish a prima facie case of obviousness is contrary to a body of law which holds that a product may be described by the process of making it. As pointed in Ex parte Goldgaber, 41 USPQ2d 1173, 1176 BPAI 1996), there is nothing intrinsically wrong in the application of methodology in the rejection product claims under 35 USC 103 depending on the particular facts of the case, the manner and context in which methodology applies and their overall logic of the rejection. Nor does Bell or Deuel issue a blanket prohibition against the application of methodology in rejecting product claims defining DNA of cDNA. It is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound. In determining obviousness, it is appropriate to consider such matters as the manner of preparation of the composition vis-a-vis the prior art, the structural similarities as well as differences between the claimed composition and that of the prior art and the presence or absence of properties which would unobvious in view of the prior art. See In re Pilkington, 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); In re Best, 562, F.2d 1252, 195 USPQ 430 (CCPA 1977). The Federal Circuit has recognized that a gene, being a chemical compound , could be defined "by its methods of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguished it (from other

materials)." See Amgen, 927 F.2d 1200 at 1206, 18 USPQ2d at 1021 (Fed. Cir., 1991); Fiers V. Sugano, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993). As noted in In re Cofer, 354, F.2d 664, 148 USPQ 268 (CCPA 1966), the particular structure or form of a chemical compound is an important consideration in determining obviousness under 35 USC 103; but it is not the only consideration.. A compound may well be defined or described by characteristics other than its chemical structure. Though those skilled in the art may be unaware of the exact chemical structure of an antibody they are aware that is it composed of established relatively unchanging (array of nucleotides which code for the particular protein) . Importantly, they are also aware that the probe will hybridize with the targeted antibody or immunoglobulin of interest. Those skilled in the art are also aware of established procedures for isolating the gene using the hybridization phenomenon. Such procedures are taught in the references of record and employed by appellant in the instant disclosure. Therefore, the ordinary artisan would have made the instant in turn, would have made the cDNA of said RFB4 antibody with a reasonable expectation of success.

The response further states that Orlandi et al points out that it is not possible to determine the exact sequence of both ends of the V genes and cites page 3837 in Orlandi et al. In response to this argument, the passage cited in Orlandi et al states that the sequence is dictated by the primer and it would have been obvious to sequence both regions and strands of the V genes using different primers as these methods are well known in the art as evidenced by the specification on pages 23-25 which teach appropriate cloning and sequencing techniques.

The response further states "the art may indicate that some dsFv immunotoxins may have superior stability and cytotoxicity, it does not predict which antibody can be stably expressed as immunoconjugates to provide superior stability and cytotoxicity" and cites Table 3 of Reiter (see page 8 of response). In response to these arguments, Table 3 of Reiter et al clearly demonstrates that in almost every case the cytotoxicity of the dsFv is better than the scFv as demonstrated by a lower IC50. In addition, Reiter et al clearly teach that the expression of the dsFv-immunotoxins are better because of the enhanced stability and have a decreased tendency to aggregate (see page 5458, right column).

The following are some NEW GROUNDS of rejection

Claim Rejections - 35 USC § 112

7. Claims 11-14, 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 11 has been amended to recite the limitation of "immunoconjugate comprising a sequence encoding for a toxin peptide and an antibody that binds to an RFB4 disulfide-stabilized Fv (dsFv)". The response filed 11/8/02 states that support for the amendment can be found at page 18, lines 12-29. The response has been carefully considured but is deemed not to be persuasive. The recited page does not disclose any antibody immunoconjugate that binds to the RFB4 dsFv. Applicant is required to

provide specific support in the application as originally filed for the limitation or remove the limitation from the claim.

Conclusions

8. No Claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00

am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879